REMARKS

Claims 17, 18, 21 to 23, 28 to 31, 34 to 42, and 46 to 52 as set forth in Appendix I of this paper are herewith presented for further prosecution. Relative to the previous version of the claims, Claims 43 to 45 have been canceled, Claims 30, 46, and 50 to 52 have been amended, and no new claims have been added, as indicated in the listing of the claims.

More specifically, Claim 30 has been revised to correct the name of the recited compound, Claim 46 has been revised to correct its dependence, and Claims 50 to 52 have been revised to correct the definition of the substituent designated as "Y", *cf. e.g.* application page 19, indicated line 15. No new matter has been added. Favorable consideration is respectfully solicited.

In light of the foregoing and the attached, Claims 17, 18, 21 to 23, 28 to 31, 34 to 42, and 46 to 52 are herewith pending in the application. Of the pending claims, Claims 17, 18, 22, 23, 31, 34, 38 to 42, 46, 49 and 52 stand withdrawn from consideration, and Claims 21, 28 to 30, 35 to 37, 47, 48, 50 and 51 stand rejected.

Claims 21, 28 to 30, 35 to 37, 47, 48, 50 and 51 were rejected as allegedly being unpatentable

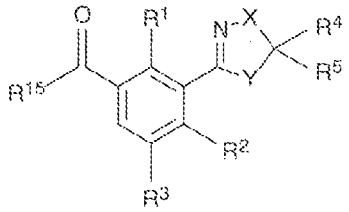
a) under 35 U.S.C. §103(a) in light of the teaching of ***von Deyn et al***. (**WO 96/26206** *which corresponds to* **US 5,846,907**) when taken in view of the disclosure of ***Silverman*** (**The Org. Chem.** *of Drug Design and Drug Action, Academic Press, Inc. San Diego, 1992, pp. 4-51*), and

b) under the judicially created doctrine of obviousness-type patenting in light of Claims 1 to 8 of ***von Deyn et al***. (**US 5,846,907**) when taken in view of the disclosure of ***Silverman*** (**The Org. Chem.** *of Drug Design and Drug Action, Academic Press, Inc. San Diego, 1992, pp. 4-51*).

For the reasons set forth in the following, the subject matter applicants' claims is not deemed to be rendered obvious by the referenced art. The analysis employed in an obviousness-type double patenting rejection parallels the guidelines for analysis of a 35 U.S.C. §103 obviousness determination, *e.g.*, *In re Braithwaite*, 379 F.2d 594 (CCPA 1967); *In re Longi*, 759 F.2d 887 (Fed. Cir. 1985); *In re Braat*, 837 F.2d 589 (Fed. Cir. 1991). Therefore, the following arguments

are applicable not only to the question of patentability under Section 103 but also to the question of patentability under the judicially created doctrine of obviousness-type double patenting.

The subject matter of Claim 28 is deemed to be representative of the subject matter delineated in Claims 21, 28 to 30, 35 to 37, 47, 48, 50 and 51. Claim 28 is drawn to a particular 3-heterocyclyl-substituted benzoyl compound of formula I



I

wherein

X is O;

R^1 is C_1-C_2-alkyl, methoxy or methylsulfonyl;

R^2 is nitro, halogen, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkylthio, C_1-C_6-alkylsulfinyl, C_1-C_6-alkylsulfonyl or C_1-C_6-haloalkylsulfonyl;

R^3 is hydrogen, halogen or C_1-C_6-alkyl;

R^4 is hydrogen or methyl, and R^5 is hydrogen;

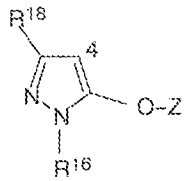
Y is $CR^{13}R^{14}$;

R^{13}, R^{14} are hydrogen, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxycarbonyl, C_1-C_4-haloalkoxycarbonyl or $CONR^7R^8$;

R^7 is hydrogen or C_1-C_4-alkyl;

R^8 is C_1-C_4-alkyl;

R^{15} is a pyrazole of formula II which is linked in the 4-position



II

wherein

R^{16} is C_1-C_6-alkyl;

Z is H; and

R^{18} is hydrogen or methyl.

Claims 29, 30, 31, 34 to 37, and 50 are drawn to embodiments of the compounds which fall within the scope of Claim 28. Claim 21 is drawn to a composition comprising at least one compound according to Claim 28, and Claims 48 and 51 are drawn to embodiments of the composition which fall within the realm of Claim 21.

The rejection applies the teaching of ***von Deyn et al***. for generically embracing compounds of applicants' formula (I) and compositions comprising those compounds, and specifically for illustrating in Examples 5.4 and 5.5 compounds which differ from those of applicants' claims in that they carry a chlorine substituent in the position designated as R^1 in applicants' formula (I). That is, the respective illustrative compounds of ***von Deyn et al***. are substituted by chlorine in a position where applicants' compounds carry a C_1-C_2-alkyl group, a methoxy group, or a methylsulfonyl group. The disclosure of ***Silverman*** is joined for allegedly describing methyl and chlorine as bioisosters which would be expected to maintain activity, and describing that alkyl groups of varying chain lengths also have similar activity. On this basis, the rejection concludes that it would have been *prima facie* obvious to one having ordinary skill to modify the illustrative compounds in Examples 5.4 and 5.5 of ***von Deyn et al***. by replacing the chlorine substituent by a C_1-C_2-alkyl group with the expectation that the resultant compounds and ***von Deyn et al***.'s compounds exhibit the same activity.

It is respectfully urged that the disclosure of ***Silverman*** fails to reasonably support the proposition for which it is applied. While it is true that Section (1.) beginning on page 16 of the reference addresses general effects which may occur upon homologation of an alkyl chain, it is specifically stated, "*Major pharmacological changes can occur with chain branching and homologation.*" *See* Section (2.), page 18, para. 2, first sentence. As an example, ***Silverman*** mentions that homologation of diethazine, an antispasmodic and antihistaminic compound, yields promazine, *i.e.*, a compound which has greatly reduced antispasmodic and antihistaminic activity whereas the sedative and tranquillizing properties are greatly enhanced. Similarly, while Table 2.2 of the reference (pages 19-20) enumerates methyl, hydroxyl, amino, fluoro and chloro radicals as "classical isosters" it is specifically noted, "*Bioisosterism also can lead to changes in activity.*" *See* page 21, first fill para., 3rd sentence. Following formula (2.35) on page 21, ***Silverman*** discusses a number of parameters which are affected by a change along the lines of bioisosterism, as well as possible effects of such a change, *i.e.*, on the binding of the compound at

the target site, on receptor binding, on pharmacokinetics, and on metabolism. Accordingly, the effect of a particular change based on bioisosterism on the effectivity of a compound cannot be predicted. The whole chapter of ***Silverman*** is focused on various approaches which may be taken to modify a lead structure in order to "*amplify the desired activity and to minimize or eliminate the unwanted properties[,]*" *see* page 4, first para., 3rd sentence. However, in spite of the knowledge regarding those approaches, the chapter concludes, "*it appears that even if one uncovers a lead, it may be a fairly random process to optimize its potency. ...*" *See* page 47, section (G), 1st sentence. When duly considered as a whole, the secondary reference therefore cannot be deemed to suggest that the exchange of a substituent following the principles of bioisosterism, and/or the homologation of an alkyl group in a lead compound *per se* can be deemed to yield a predictable result.

In this context it is also deemed to be pertinent to bear in mind that ***van Deyn et al.***'s Tables 1 and 5 enumerate a multitude of compounds with varying substituents in the positions R^1, R^2, R^3, M, Z and L of the prior art formula. One having ordinary skill in the art who sought to modify the illustrative compounds of ***von Deyn et al.*** would not have been advised by the disclosure of ***Silverman*** how to do so with the necessary reasonable expectation of success. At the least, such a person would have had to:

1. select ***von Deyn et al.***'s illustrative Examples 5.4 and 5.5 as lead compounds from the multitude of compounds which are specifically enumerated in the reference;
2. select the position R^1 from among the positions R^1, R^2, R^3, M, Z and L of the prior art formula as a position suitable for modification; and
3. select the approach via bioisosterism from the various approaches discussed by ***Silverman***.

Neither the teaching of ***von Deyn et al.*** nor the disclosure of ***Silverman*** can be deemed to provide information which would have guided one of ordinary skill in the direction necessary to arrive at the compounds encompassed by applicants' claims. There is nothing in the teaching of ***von Deyn et al.***, taken along or taken together with the disclosure of ***Silverman***, which suggests or implies the suitability of the compounds of prior art Examples 5.4 and 5.5 as lead structures. For example, none of the varying locations of the substituents of the prior art compounds, *i.e.*, none of the positions R^1, R^2, R^3, M, Z and L of the prior art formula, is identified or suggested as a variable which is of particular result effectivity, *i.e.*, all positions are equivalent in their effectivity with a view to improving the properties of the prior art compounds. As such, the teaching of ***von Deyn et al.***, taken alone or taken in view of the disclosure of ***Silverman***, fails to

suggest or reasonably imply the position of R^1 as a site for a particular structural modification. Similarly, the conclusion of ***Silverman*** in section (G) of the reference further emphasizes that one of ordinary skill had no way of discerning which of the many possible choices may reasonably be expected to be successful. Under certain circumstances, what is "*obvious to try*" may be equated with obviousness, namely, where the prior art provided a finite number of identified, predictable potential solutions to a recognized need or problems. *See KSR Int'l v. Teleflex, Inc.*, 550 U.S. 398, 421 (2007). However, "*"obvious to try" is erroneously equated with obviousness under Section 103(a) where 'what would have been "obvious to try" would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful.'*" *See In re Kubin*, 561 F.3d 1351, 1359 (2009) (quoting *In re O'Farrell*, 853 F.2d 894, 903 (Fed. Cir. 1988). As such, the teaching of ***von Deyn et al***. taken alone or taken in view of the disclosure of ***Silverman*** cannot be deemed to render the subject matter of applicants' claims obvious within the meaning of Section 103(a).

The rejection *inter alia* argued that one of ordinary skill would consider it routine and well within their technical grasp to alter the substituents and screen the modified structures for activity on a large scale to improve the properties. Applicants respectfully urge that Section 103(a) specifically states: "*Patentability shall not be negatived by the manner in which the invention was made*." Accordingly, the path that leads an inventor to the invention is expressly made irrelevant to patentability by statute. In fact, the Court has stated: "*Most technological advance is the fruit of methodical, persistent investigation as is recognized in 35 U.S.C. §103 ('patentability shall not be negatived by the manner in which the invention was made')*." *In re Dow Chemical Co.*, 837 F.2d 469, 472 (Fed. Cir. 1988). The mere fact that one may be able to find a structural modification of the compounds of ***von Deyn et al***. which conveys to the compounds particular properties by using routine and ordinary skill is therefore clearly without relevance in the determination whether the structurally modified compounds are patentable under the provisions of Section 103(a).

The rejection erroneously asserts that the record does not contain evidence of secondary considerations. Applicants have provided two Declarations of Dr. Witschel, both executed on October 21, 1999, and both presented with applicants' paper of October 25, 1999. Supplemental copies of the Declarations are herewith enclosed for the Examiner's convenience. The first of the

two Declarations, in particular, investigates the herbicidal activity of the 4,5-dihydroisoxazol-3-yl-substituted benzoylpyrazoles Nos. 5.4 and 5.5 (*col. 29 of* **US-A 5,846,907**) and No. 1.267 of ***WO-A 96/26,206*** (*corresponds to compound No. 1.79, col. 18 of* **US-A 5,846,907**) and the activity of those compounds within applicants' claims which come structurally closest to these prior art compounds.

It is immediately apparent when the herbicidal effectivity of applicants' compounds and of the prior art compounds is compared (*ie. the data set forth in Tables 1 and 2, pages 2 and 3, of Dr. Witschel's Declaration*) that a sufficient effect against unwanted plants can only be achieved with the prior art compounds at application rates which cause significant harm to the crop plant. However, the structurally closest compounds of applicants' invention are well tolerated by the crop plants and have a high(er) effectivity against the unwanted plants. The beneficial effect becomes even more pronounced, e.g., when the effectivity of applicants' compound 3.90 at an application rate of 31.2 g/ha is compared with the effectivity of ***von Deyn et al.***'s compound No. 5.5 at an application rate of 62.5 g/ha. Applicants' compound yields a better herbicidal effect than the prior art compound although the application rate of the compounds according to the present invention is reduced by half compared to the application rate of the prior art compound. A comparison of the herbicidal effect of applicants' compounds ***A*** and ***B*** and the prior art compounds Nos. 5.4 and No. 1.267 (*or No. 1.79 as this compound is designated in the corresponding U.S. patent*) of ***von Deyn et al***. further corroborate the distinct and unexpected improvement of the herbicidal effects of applicants' compounds (*see Tables 3 and 4, pages 3 and 4, of Dr. Witschel's Declaration*). Additionally, the investigations and data compiled in Dr. Witschel's second Declaration corroborate that the improved herbicidal efficacy of applicants' compounds is not limited to those compounds which come structurally closest to the prior art compounds.

For at least the foregoing reasons, applicants' Claims 21, 28 to 30, 35 to 37, 47, 48, 50 and 51 are patentable under the provisions of Section 103(a), and correspondingly under the judicially created doctrine of obviousness-type double patenting, in light of the teaching of ***von Deyn et al***. when taken in view of the disclosure of ***Silverman***. It is therefore respectfully requested that the rejections be withdrawn. Favorable action is solicited.

The Office action reiterated the restriction requirement noting, in addition to the reasons provided in the previous proceedings, that examination of the groups of claims together would

require multiple searches further emphasizing that there would be an undue burden on the examiner. Applicants respectfully urge that the application was filed under Section 371 as a national stage of international application PCT/EP 98/00069. As such, the guidelines of MPEP Chapter 800 are not applicable in the present application, *cf.* MPEP §801. The burden on the examiner is not a criterion which applies in a determination of unity of invention under PCT Rule 13 or 37 C.F.R. §1.475, *cf.* MPEP Chapter 1875. Applicants therefore respectfully reiterate their request that the restriction requirement be withdrawn. Favorable action is solicited.

In light of the foregoing and the attached, the subject matter defined in in applicants' claims is deemed to be patentable under the pertinent provisions, and the application meets the requirements relating to the form or contents which are applicable in the present case. Allowance of the application should therefore be equitable. Favorable action is solicited.